



## Postoperative mortality in elderly patients with colorectal cancer: The impact of age, time-trends and competing risks of dying



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### ABSTRACT

**Background:** Worse prognosis in elderly colorectal cancer (CRC) patients may be cancer or treatment related, or death from other causes. This population-based study aimed to compare survival among non-metastatic CRC patients between age groups and notice time trends in mortality rates.

**Methods:** Primary stage I–III CRC patients who underwent resection between 2008 and 2013 were selected from the Netherlands Cancer Registry. Patients were divided into three equally distributed age groups and a separated group including the oldest old (<65, 65–74, 75–84 and ≥85 years). Survival rates were calculated by age groups and tumour localization. Relative excess risks of death, 30-day, 1-year mortality and 1-year excess mortality were calculated.

**Results:** 52296 patients were included. Age-related differences in 5-year overall survival were observed (colon cancer: 82%, 73%, 56% and 35%; rectal cancer: 82%, 74%, 56% and 38%;  $p < 0.0001$ ). Age-related differences were less prominent in relative survival and disappeared in conditional relative survival (condition of surviving 1 year). Thirty-day mortality rates decreased over time (colon cancer: 4.9%–3.4%; rectal cancer: 3.0%–1.7%); 1-year mortality rates decreased from 11.9% to 9.6% in colon cancer and from 8.0% to 6.4% in rectal cancer. One-year excess mortality increased with age (17.3% and 12.9% in patients with colon or rectal cancer aged ≥85 years).

**Conclusion:** One-year mortality rates remain high in elderly patients. Age-related differences in survival disappeared after adjustment for expected death from other causes and first-year mortality. Beneficial time trends in 1-year mortality rates underline that survival in elderly after CRC surgery is modifiable.

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### Introduction

Nowadays more than 50% of colorectal cancer (CRC) is being diagnosed in patients over 70 years of age [1]. The incidence of CRC in the Dutch population is still increasing rapidly due to ageing of the population and the introduction of the Dutch CRC screening program [2].

Surgery is the cornerstone treatment in stage I–III CRC patients.

Compared to younger patients, in the elderly excess mortality after surgical interventions does not only occur in the first postoperative month but in the first postoperative year. A previous population-based study showed an overall mortality of 20–23% in elderly patients (aged ≥75 years) within the first postoperative year after colorectal surgery. A significant excess mortality one year after surgical resection (16% for colon cancer and 13% for rectal cancer) was found in the oldest age groups [3]. After the first postoperative year, elderly CRC patients had similar relative survival (RS) compared to younger patients.

During the past decades many developments in peri-operative care have been made: surgical techniques have changed, i.e. the introduction of minimally invasive endoscopic surgery [4–6]. Also

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referral of patients to high-volume centers and differentiation of surgical areas has increased [7,8]. Furthermore peri-operative care has been improved by introducing enhanced recovery programs, and for frail elderly patients a pre-operative comprehensive geriatric assessment (CGA) has been developed [9].

The primary aim of this study was to evaluate population-based survival data for young (<65 years), aged (65–74 years), elderly (75–84 years) and the oldest old patients ( $\geq 85$  years) with stage I–III CRC who underwent surgery in the period 2008–2013 in the Netherlands.

## Patients and methods

Data from the nationwide Netherlands Cancer Registry (NCR) were used, managed by the Netherlands Comprehensive Cancer Organisation (IKNL). Information on patient and tumour characteristics, diagnosis and treatment is routinely extracted from the medical records. The quality of the data is high due to thorough training of the registration team and computerised consistency checks at regional and national level.

Anatomical site of the tumour is registered according to the International Classification of Disease – Oncology (ICD-O) [10]. The TNM (tumour-node-metastasis) classification is used for stage notification of the primary tumour, according to the edition valid at time of cancer diagnosis [11].

Population-based data from the NCR in the Eindhoven area were used for a sub analysis to provide data on comorbidities for this study. This region records data on all newly diagnosed cancer patients in the south-eastern part of the Netherlands. Comorbidities are registered according to a slightly modified version of the Charlson Comorbidity index [12]. Comorbid diseases were defined as life shortening diseases present at the time of CRC diagnosis.

## Study population

All patients who underwent surgical resection for primary stage I–III CRC (C18–20) between 2008 and 2013 were included. Patients were excluded if they had an unknown stage of disease ( $n = 633$ ), if they were treated with local tumour destruction (polypectomy, transanal endoscopic microsurgery (TEM), transanal excision (TAE)) ( $n = 2855$ ) or if date of resection was missing ( $n = 46$ ).

Stage was based on the pathological TNM classification; clinical information was used if pathology data were missing. Patients were stratified by tumour localization: colon (C18) and rectum (rectosigmoid and rectum, C19–C20). Patients were divided into age groups: <65, 65–74, 75–84 and  $\geq 85$  years. The oldest age category was based on the selection of the oldest old of the CRC patients while the other age categories were chosen to create equal distributions of patients between age groups. Primary treatment of colon cancer was classified as surgery, surgery with adjuvant chemotherapy or other. Rectal cancer treatments were classified as surgery, surgery with neoadjuvant radiotherapy, surgery with neoadjuvant chemoradiotherapy or other. Furthermore, detailed information was available on urgency of the resection (emergency resection <24 h after presentation) for patients with colon cancer.

Patients' vital status was obtained by linking the NCR to the Municipal Personal Records Database (GBA). Follow-up was completed until January 1st, 2018.

## Survival definitions

Survival was defined as the time from the date of resection to the date of death or last follow-up date (January 1, 2018) for patients who were still alive.

Overall survival (OS) was defined as the probability of surviving

from all causes of death. Relative survival (RS) was calculated as the ratio of the survival observed among the cancer patients and the survival that would have been expected based on the corresponding (age, gender and year) general population [13]. Conditional survival (CRS) was defined as the relative survival among patients who survived the first year after surgical resection.

## Statistical analyses

Differences in patient and tumour characteristics across the different age groups were evaluated using Chi<sup>2</sup>-tests after stratification by tumour localization.

OS was calculated using the Kaplan-Meier method. Furthermore, RS and CRS were calculated using the Pohar Perme method [14].

Relative excess risks of death (RER) were estimated using a multivariable generalized linear model with a Poisson distribution, based on collapsed relative survival data, using exact survival times, adjusting for gender, age, period of diagnosis, stage, treatment and emergency of resection (the latter only for colon cancer). Post-operative 30-day and 1-year mortality were calculated as well as the 1-year excess mortality (observed-expected deaths/number of patients).

*P* values below 0.05 were considered statistically significant. Analyses were performed in STATA (version 13.0, Statcorp LP, College Station, TX).

## Results

Over the period 2008–2013, 52296 patients were diagnosed with primary non-metastatic CRC and underwent surgical resection: 36464 colon cancer patients and 15832 rectal cancer patients. Table 1 shows the distribution of patient- and tumour characteristics by age groups and tumour localization.

## Survival

Median follow-up time for patients included was 60 months. Differences in 5-year OS were observed between age groups ( $p < 0.0001$ , Fig. 1a). Differences in survival between the age groups were less prominent in RS, however, advanced age still reduced RS (Fig. 1b). The age-related differences disappeared in CRS (Fig. 1c).

For colon cancer, analyses were repeated excluding patients who underwent emergency resection ( $n = 2767$ ). Higher 5-year survival rates for OS, RS and CRS among patients who underwent elective surgical resection were observed, compared to the overall study population. Furthermore, age-related differences on survival did not change (data not shown).

## Relative excess risks of death

An increased RER of death was observed in the elderly as compared to younger patients for colon and rectal cancer. When RER was calculated for patients who survived the first year after surgical resection, differences in RER disappeared for all age groups for colon and rectal cancer (Table 2). When analyses were repeated with the older age groups taken together as one group, similar results were found for colon cancer (RER CRS  $\geq 75$  versus <65 years 1.0 (0.88–1.14)) and rectal cancer (RER CRS  $\geq 75$  versus <65 years 1.4 (0.94–1.48)).

Analyses were repeated including patients of the Eindhoven area ( $n = 7495$ ). Age-related differences in RER for RS and CRS disappeared after adjustment for the number of comorbidities among patients with colon cancer (Table 3). For rectal cancer, an increased risk of death remained in the older age groups with a

**Table 1**

Patient and tumour characteristics of patients who underwent surgical resection for stage I–III colon or rectal cancer diagnosed in the period 2008–2013 according to age (n = 52296).

	<65 years n (%)	65–74 years n (%)	75–84 years n (%)	≥85 years n (%)	p-value
<b>COLON CANCER</b>					
<b>Total</b>	9847 (27)	11607 (32)	11775 (32)	3235 (9)	
<b>Gender</b>					<0.0001
Male	5263 (53)	6393 (55)	5813 (49)	1265 (39)	
Female	4584 (47)	5214 (45)	5962 (51)	1970 (61)	
<b>Period of diagnosis</b>					<0.0001
2008–2009	3293 (33)	3555 (31)	3770 (32)	1088 (33)	
2010–2011	3311 (34)	3853 (33)	3993 (34)	1122 (35)	
2012–2013	3243 (33)	4199 (36)	4012 (34)	1025 (32)	
<b>Stage</b>					<0.0001
Stage I	1887 (19)	2599 (22)	2482 (21)	533 (16)	
Stage II	3831 (39)	4758 (41)	5399 (46)	1610 (50)	
Stage III	4129 (42)	4250 (37)	3894 (33)	1092 (34)	
<b>Treatment</b>					<0.0001
Surgery only	5369 (55)	7836 (67)	10396 (88)	3213 (99)	
Surgery + adjuvant CT	4366 (44)	3665 (32)	1313 (11)	15 (0.5)	
Other <sup>d</sup>	112 (1)	106 (1)	66 (1)	7 (0.5)	
<b>Emergency resection<sup>a</sup></b>					<0.0001
Emergent	849 (9)	783 (7)	794 (7)	347 (11)	
Elective	8830 (91)	10660 (93)	10842 (93)	2836 (89)	
<b>Surgical procedure<sup>b</sup></b>					<0.0001
Open resection	6063 (62)	7351 (64)	8160 (70)	2455 (76)	
Laparoscopic resection	3687 (38)	4166 (36)	3534 (30)	757 (24)	
<b>Number of comorbidities<sup>c</sup></b>					<0.0001
0	690 (49)	416 (24)	261 (15)	51 (13)	
1	393 (28)	487 (28)	390 (23)	97 (24)	
≥2	331 (23)	812 (48)	1044 (62)	253 (63)	
<b>RECTAL CANCER</b>					
<b>Total</b>	6209 (39)	5385 (34)	3612 (23)	626 (4)	
<b>Gender</b>					<0.0001
Male	3851 (62)	3537 (66)	2109 (58)	298 (47)	
Female	2358 (38)	1848 (34)	1503 (42)	328 (53)	
<b>Period of diagnosis</b>					<0.0001
2008–2009	2099 (33)	1700 (31)	1204 (33)	232 (37)	
2010–2011	2106 (34)	1822 (34)	1186 (33)	227 (36)	
2012–2013	2004 (33)	1863 (35)	1222 (34)	167 (27)	
<b>Stage</b>					<0.0001
Stage I	1015 (16)	1046 (19)	735 (20)	131 (21)	
Stage II	1417 (23)	1397 (26)	1157 (32)	225 (36)	
Stage III	3777 (61)	2942 (55)	1720 (48)	270 (43)	
<b>Treatment</b>					<0.0001
Surgery only	590 (10)	759 (14)	888 (25)	293 (47)	
Surgery + neoadjuvant RT	2593 (42)	2518 (47)	2026 (56)	314 (50)	
Surgery + neoadjuvant CRT	2725 (43)	1892 (35)	630 (17)	19 (3)	
Other <sup>d</sup>	301 (5)	216 (4)	68 (2)	0 (0)	
<b>Surgical procedure<sup>b</sup></b>					<0.0001
Open resection	3632 (59)	3327 (62)	2305 (64)	438 (70)	
Laparoscopic resection	2490 (41)	1987 (38)	1276 (36)	184 (30)	
	<65 years n (%)	65–74 years n (%)	75–84 years n (%)	≥85 years n (%)	p-value
<b>Number of comorbidities<sup>c</sup></b>					<0.0001
0	486 (57)	256 (32)	100 (19)	7 (11)	
1	231 (27)	268 (33)	153 (28)	17 (24)	
≥2	147 (16)	273 (35)	287 (53)	45 (65)	

CT chemotherapy, RT radiotherapy, CRT chemoradiotherapy.

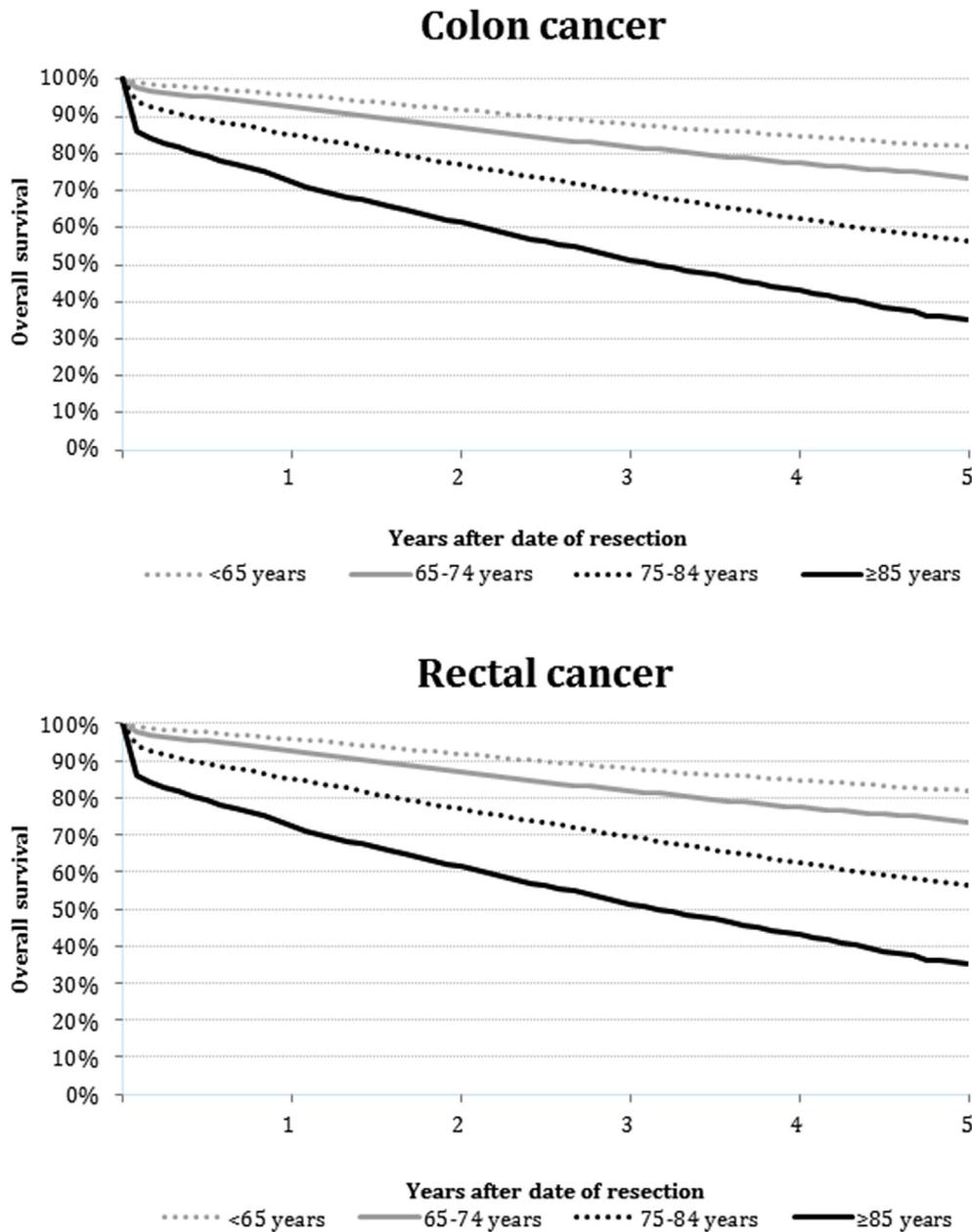
<sup>a</sup> Included in the analysis but results not shown emergency resection unknown (n = 168).<sup>b</sup> Included in the analysis but results not shown surgical approach unknown (n = 484).<sup>c</sup> Included stage I–III CRC patients diagnosed in the south-eastern part of the Netherlands and who underwent surgical resection (n = 7495).<sup>d</sup> Other (colon cancer): surgery with adjuvant radiotherapy, chemotherapy followed by radiotherapy or surgery with.

more pronounced association in the oldest old age group. RER CRS did not differ between age groups.

#### Excess mortality

Table 4 shows risk factors for overall postoperative 30-day and 1-year mortality, and 1-year excess mortality by tumour

localization. Postoperative 1-year mortality rates doubled or tripled compared to postoperative 30-day mortality rates. For both colon and rectal cancer patients, age, tumour stage, surgical approach and number of comorbidities were significant factors for postoperative 30-day and 1-year mortality ( $p < 0.0001$  for all variables) (Table 4). Additionally, increased 30-day and 1-year mortality rates were observed when colon cancer patients underwent an emergency



**Fig. 1.** Overall survival according to age of patients who underwent surgical resection for stage I–III colon or rectal cancer ( $n = 52296$ ) (a), relative survival according to age of patients who underwent surgical resection for stage I–III colon or rectal cancer ( $n = 52296$ ) (b), conditional survival according to age of patients who underwent surgical resection for stage I–III colon or rectal cancer ( $n = 47293$ ) (c).

resection ( $p < 0.0001$ ). Furthermore, 30-day and 1-year mortality rates decreased over the period of diagnosis 2008–2009, 2010–2011 and 2012–2013. For colon cancer patients, the postoperative 30-day mortality rates were 4.9%, 4.2% and 3.4% and the 1-year mortality rates were 11.9%, 10.5% and 9.6% respectively, while for rectal cancer patients the proportions of postoperative 30-day mortality were 3.0%, 2.3% and 1.7% and the 1-year mortality rates were 8.0%, 7.0% and 6.4%.

The excess mortality one year after surgical resection was highest in the older age groups, in patients with stage III CRC tumours and when patients underwent open resection for both colon and rectal cancer. Moreover, colon cancer patients undergoing emergency resection had high excess mortality. Subanalysis

showed that patients with two or more concomitant diseases present at diagnosis had highest excess mortality.

Analyses were repeated with the older age groups taken together as one group ( $\geq 75$  years). For colon cancer patients, the postoperative 30-day mortality and 1-year mortality rates in this age group were 7.7% and 17.6%, respectively, while for rectal cancer patients the postoperative mortality rates were 5.5% and 14.8%. The proportions of excess mortality one year after surgical resection in this age group were 11.9% for colon cancer patients and 9.5% for rectal cancer patients.

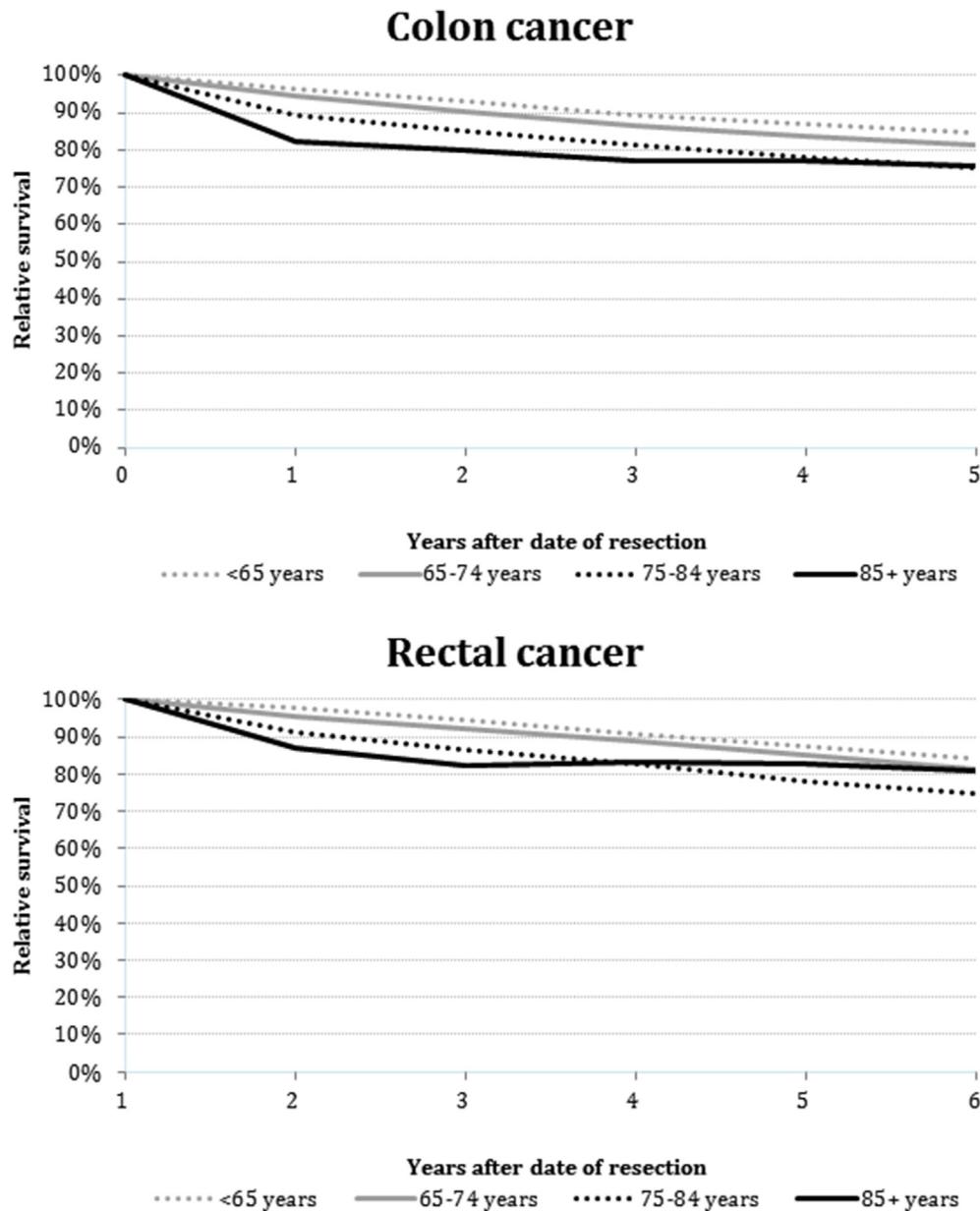


Fig. 1. (continued).

## Discussion

In this nationwide population-based study, we analysed survival differences of patients with non-metastatic CRC between different age groups. It considers overall-, relative- and conditional relative survival. We found that the substantial age-related differences in survival rates present in OS, were less prominent in 5-year RS and disappeared in 5-year CRS among the different age groups.

Postoperative mortality was higher with increasing age; after one year, almost a quarter (27.3% for colon cancer and 23.1% for rectal cancer) of the patients in the oldest age group had died. Thus, there is a substantial high mortality rate during the first postoperative year and surgery has a prolonged impact on survival. These findings are in accordance with previous studies [2,3,15–17].

In a previous Dutch study by Dekker et al., postoperative 1-year mortality rates were higher compared to our study for both colon as well as rectal cancer patients aged 75 years and older (colon cancer:

23.2% versus 17.6%, and rectal cancer: 20.1% versus 14.8%). Thirty-day mortality rates in patients aged 75 years or older were more or less comparable between the studies (colon cancer: 7.7% versus 7.5%, and rectal cancer: 5.5% versus 3.7%) [3]. Unfortunately, data on emergency resection were not available in the study of Dekker et al. We hypothesize that CRC patients undergoing emergency procedures have more advanced cancer. The higher mortality rates among these patients may be either caused by the malignancy of the tumour or a complication of the treatment. The decrease in postoperative 1-year mortality over the years may reflect a period effect due to changes in selection, surgical techniques or peri- and postoperative care in elderly patients. Laparoscopic techniques are now widely implemented. Several meta-analyses or RCT's on postoperative mortality comparing open versus laparoscopic techniques showed a non-significant trend in favor of laparoscopic surgery [18,19]. Recently, Gietelink et al. showed in a large population-based study that especially in elderly and frail patients

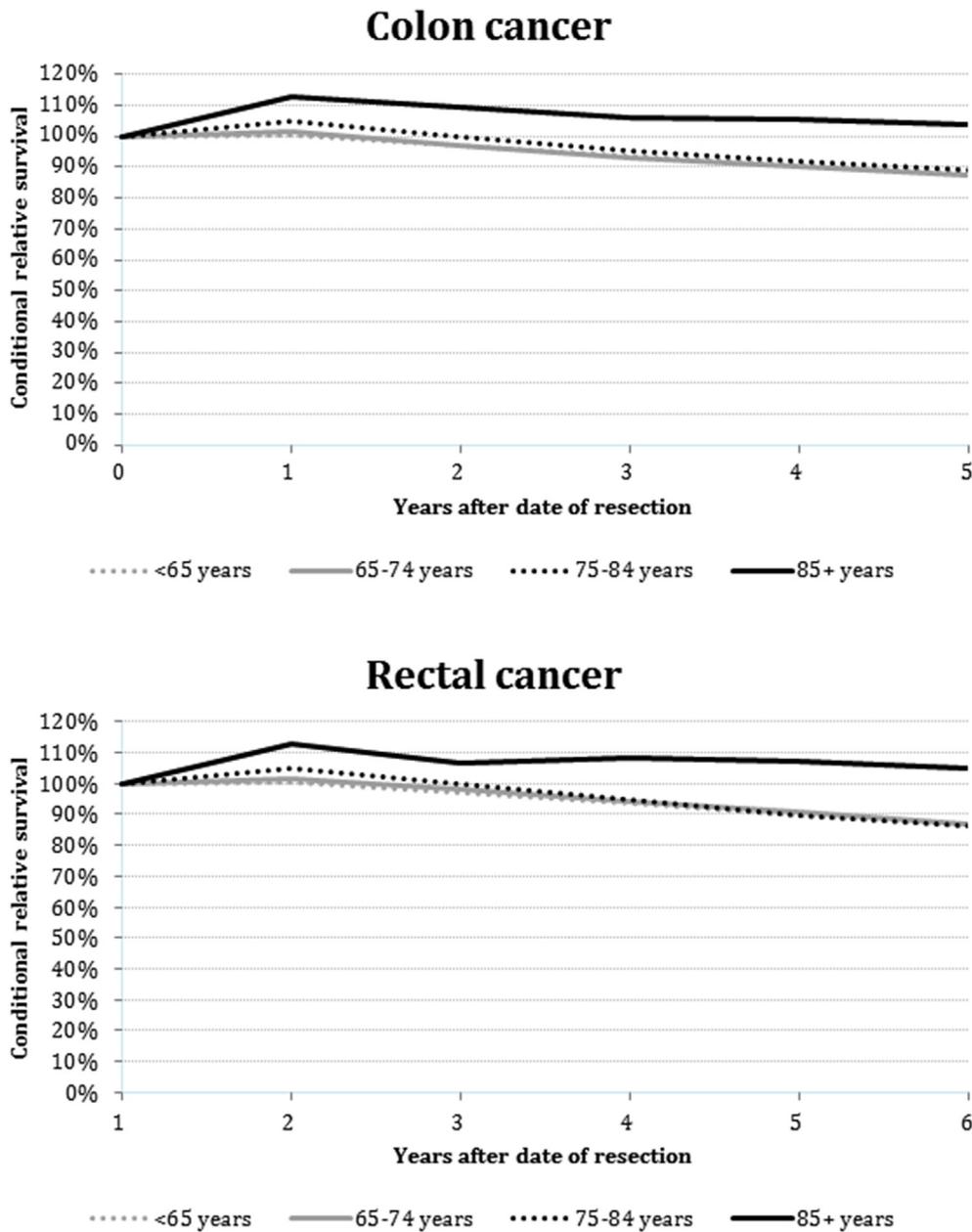


Fig. 1. (continued).

**Table 2**  
Relative Excess Risks of death (RER) for relative and conditional relative survival of patients who underwent surgical resection for stage I-III colon or rectal cancer diagnosed in the period 2008–2013 according to age (n = 52296).

	RS	95% CI	CRS	95% CI
<b>COLON CANCER</b>				
<65 years	reference		reference	
65–74 years	<b>1.2</b>	<b>1.13–1.32</b>	1.1	1.00–1.21
75–84 years	<b>1.7</b>	<b>1.56–1.83</b>	1.1	0.95–1.20
≥85 years	<b>2.1</b>	<b>1.80–2.38</b>	1.1	0.98–1.76
<b>RECTAL CANCER</b>				
<65 years	reference		reference	
65–74 years	<b>1.2</b>	<b>1.03–1.29</b>	1.0	0.96–1.25
75–84 years	<b>1.7</b>	<b>1.50–1.94</b>	1.1	0.99–1.79
≥85 years	<b>2.1</b>	<b>1.24–3.65</b>	1.1	0.46–1.96

RS relative survival, CRS conditional relative survival, CI confidence interval.  
<sup>2</sup> Adjusted for gender, period of diagnosis, stage, treatment, surgical approach and emergency of resection (the latter for colon cancer only).

**Table 3**  
Relative Excess Risks of death (RER) for relative and conditional relative survival of patients who underwent surgical resection for stage I-III colon or rectal cancer diagnosed in the period 2008–2013, in the south-eastern part of the Netherlands, according to age (n = 7495).

	RS	95% CI	CRS	95% CI
<b>COLON CANCER</b>				
<65 years	reference		reference	
65–74 years	1.1	0.86–1.33	1.0	0.77–1.30
75–84 years	1.1	0.88–1.41	0.9	0.69–1.28
≥85 years	1.2	0.84–1.67	0.6	0.29–1.22
<b>RECTAL CANCER</b>				
<65 years	reference		reference	
65–74 years	1.2	0.89–1.66	1.0	0.65–1.38
75–84 years	<b>2.1</b>	<b>1.54–2.95</b>	1.8	0.97–2.64
≥85 years	<b>4.5</b>	<b>2.52–7.90</b>	1.6	0.42–5.88

RS relative survival, CRS conditional relative survival, CI confidence interval.  
<sup>2</sup> Adjusted for gender, period of diagnosis, stage, treatment, number of comorbidities, surgical approach and emergency of resection (the latter for colon cancer only).

**Table 4**

Overall 30-day mortality, 1-year mortality and excess mortality rates of patients who underwent surgical resection for stage I–III colon or rectal cancer diagnosed in the period 2008–2013 according to age (n = 52296).

	n	Postoperative mortality (%)				Excess mortality (%)
		<30 days	p-value	1st year	p-value	1st year
<b>Colon cancer</b>						
<b>Overall</b>	36464	4.2		10.7		
<b>Gender</b>			0.054		0.084	
Male	18734	4.4		10.9		7.7
Female	17730	3.9		10.3		7.7
<b>Age</b>			<0.0001		<0.0001	
<65 years	9847	1.0		4.1		3.6
65–74 years	11607	2.2		7.2		5.7
75–84 years	11775	6.0		14.8		10.5
≥85 years	3235	13.8		27.3		17.3
<b>Stage</b>			<0.0001		<0.0001	
Stage I	7501	3.3		6.7		3.8
Stage II	15598	4.3		9.5		6.3
Stage III	13365	4.4		14.1		11.5
<b>Emergency resection †</b>			<0.0001		<0.0001	
Emergent	2773	11.9		23.2		20.7
Elective	33168	3.5		9.6		6.5
<b>Surgical approach</b>			<0.0001		<0.0001	
Open resection	24029	5.4		13.3		10.2
Laparoscopic resection	12144	1.8		5.5		2.8
<b>Number of comorbidities</b>			<0.0001		<0.0001	
0	1418	1.8		4.9		3.0
1	1367	2.8		7.0		4.3
≥2	2440	5.7		14.8		11.3
<b>Rectal cancer</b>						
<b>Overall</b>	15832	2.3		7.1		
<b>Gender</b>			<0.0001		<0.0001	
Male	9795	2.8		7.8		5.5
Female	6037	1.7		5.8		3.9
<b>Age</b>			<0.0001		<0.0001	
<65 years	6209	0.6		2.7		2.2
65–74 years	5385	1.8		6.0		4.4
75–84 years	3612	4.7		13.2		8.9
≥85 years	626	10.1		23.1		12.9
<b>Stage</b>			<0.0001		<0.0001	
Stage I	2927	2.4		5.3		2.9
Stage II	4196	2.8		8.0		5.5
Stage III	8709	2.1		7.4		5.4
<b>Surgical approach</b>			<0.0001		<0.0001	
Open resection	9702	3.0		8.4		6.1
Laparoscopic resection	5937	1.4		5.0		2.9
<b>Number of comorbidities</b>			<0.0001		<0.0001	
0	849	0.7		4.1		2.7
1	669	1.7		5.6		3.6
≥2	752	5.2		14.0		11.1

n/a not analysed.

\* Included in the analysis but results not shown emergency resection unknown (n = 168).

\*\* Included in the analysis but results not shown surgical approach unknown (n = 484).

\*\*\* Included stage I–III CRC patients diagnosed in the south-eastern part of the Netherland and who underwent surgical resection (n = 7495).

laparoscopic resection reduced the risk of postoperative 30-day mortality by reducing cardiopulmonary postoperative complications [20]. The excess of deaths within 1-year probably reflects a complex interaction between major surgery, comorbidities, physiologic reserve-capacity, resilience of elderly patients, and eliminating the malignant disease. It has been shown that, with increasing age, not only mortality but also postoperative morbidity increases [4,21]. This may induce a delayed and indirect effect on mortality unrolling yet in several months after surgery.

We found higher rates of excess mortality in the first postoperative year among older patients, patients with stage III CRC, patients with comorbidities and patients whom underwent an emergency resection. These findings are comparable with previous studies, in which significant risk factors for 1-year mortality were identified: comorbidities, stage III CRC, emergency resection, postoperative surgical complications, and a prolonged

postoperative hospital stay [22–26]. Furthermore, a study by Morris et al. showed that in CRC patients diagnosed in England, Sweden or Norway, the excess mortality was most evident within the first 3 months after diagnosis and for the oldest patients [27].

OS is defined as the probability of surviving from all causes of death and therefore may overestimate the impact of cancer on survival. Therefore, RS is used to adjust for mortality due to other causes than cancer. Results of this study showed that 5-year RS for patients aged 75 years and older was worse than for patients younger than 75 years. In our study, CRS in the oldest old patients (≥85 years) remained above 100% once patients survived the first postoperative year. This effect probably reflects the selection of the fittest or most resilient in this age group by CRC surgery and its recovery process.

In line with previous studies [3,22], adjusted RERs for CRS did not differ along the age-groups, indicating that differences between

survival rates are determined by mortality in the first postoperative year. Since postoperative complications are a more probable cause for early mortality, one can conclude that CRC itself is not the main cause of the age-related differences in survival [28]. Moreover, other studies found no differences in long-term cancer-specific survival between different age groups among patients with CRC [29,30].

Adjusted RERs for RS revealed a different impact of the presence of comorbidities on colon and rectal cancer survival in the older age groups ( $\geq 75$  years). In elderly colon cancer patients ( $\geq 75$  years) differences in RERs for RS disappeared after adjustment for the number of comorbidities; however, in rectal cancer patients age-related differences in RS remained. Apparently, the interaction between cancer stage, surgical interventions and comorbidities is more life threatening in rectal cancer. A major impact of the surgical procedure itself or an increase in complication rate induced by combining surgery and radiation therapy in rectal cancer may be underlying. A previous Dutch population-based study supports the latter explanation [31].

The main strength of this study is that we used a large dataset including more than 50000 CRC patients, of which almost 4000 patients were 85 years or older. The observational nature of population-based studies provides a unique insight into the effects of treatments in everyday clinical practice [32–34]. The NCR allows the evaluation of outcomes in the general patient population and provides information regarding the use, safety and outcomes in the real world. Furthermore, information on emergency resection and comorbidities is present in our dataset, making it possible to take these variables into account in multivariable analyses.

Nevertheless, results of this study should be interpreted with consideration of certain limitations. Previous studies identified postoperative complications as risk factors for death during the first postoperative year [17,22]. Unfortunately, data on postoperative complications were not available in the NCR. Also, in patients with rectal cancer a shift towards other surgical procedures may occur, especially in the very old, i.e. Hartmann's procedure. This might affect the incidence of postoperative complication and mortality as clinicians assume a lesser risk for complications with this procedure. Furthermore, our population-based study limits comparisons, either direct between subgroups/characteristics within the study population or indirect with historical population-based data. Especially risk of selection bias and omitting of relevant parameters may occur. For instance data on frailty or dependency of patients are lacking in the NCR. Both are not covered by information on the presence of comorbidities at cancer diagnosis, and are associated with complications and postoperative mortality [35].

Results of this study showed that mortality, especially within the first year after surgery remains high in patients aged  $\geq 75$  years. Age-related differences in survival disappeared after adjustment for expected death from other causes and 1-year mortality. This suggests that surgery has a greater and prolonged impact on survival postoperatively in elderly. Although our study cannot determine which factors determined this improvement, it underlines survival in elderly after major surgery is modifiable.

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## References

- [1] Ugolini G, Ghignone F, Zattoni D, Veronese G, Montroni I. Personalized surgical management of colorectal cancer in elderly population. *World J Gastroenterol* 2014;20(14):3762–77.
- [2] Visser BC, Keegan H, Martin M, Wren SM. Death after colectomy: it's later than we think. *Arch Surg* 2009;144(11):1021–7.
- [3] Dekker JW, van den Broek CB, Bastiaannet E, van de Geest LG, Tollenaar RA, Liefers GJ. Importance of the first postoperative year in the prognosis of elderly colorectal cancer patients. *Ann Surg Oncol* 2011;18(6):1533–9.
- [4] Rutten HJ, den Dulk M, Lemmens VE, van de Velde CJ, Marijnen CA. Controversies of total mesorectal excision for rectal cancer in elderly patients. *Lancet Oncol* 2008;9(5):494–501.
- [5] Huscher CG, Bretagnol F, Corcione F. Laparoscopic colorectal cancer resection in high-volume surgical centers: long-term outcomes from the LAPCOLON group trial. *World J Surg* 2015;39(8):2045–51.
- [6] Zheng Z, Jemal A, Lin CC, Hu CY, Chang GJ. Comparative effectiveness of laparoscopy vs open colectomy among nonmetastatic colon cancer patients: an analysis using the National Cancer Data Base. *J Natl Cancer Inst* 2015;107(3).
- [7] Oliphant R, Nicholson GA, Horgan PG, McMillan DC, Morrison DS. West of Scotland Colorectal Cancer Managed Clinical N. The impact of surgical specialisation on survival following elective colon cancer surgery. *Int J Colorectal Dis* 2014;29(9):1143–50.
- [8] Buurma M, Kroon HM, Reimers MS, Neijenhuis PA. Influence of individual surgeon volume on oncological outcome of colorectal cancer surgery. *Int J Surg Oncol* 2015;2015:464570.
- [9] Odagiri H, Yasunaga H, Matsui H, Fushimi K, Iizuka T, Kaise M. Hospital volume and the occurrence of bleeding and perforation after colorectal endoscopic submucosal dissection: analysis of a national administrative database in Japan. *Dis Colon Rectum* 2015;58(6):597–603.
- [10] Fritz APC, Jack A, et al. International classification of diseases for Oncology (ICD-O). Geneva: World Health Organisation; 2000.
- [11] Wittekind CGF, Hutter R, Klimpfinger M, Sobin L. TNM atlas. Berlin: Springer-Verlag; 2004.
- [12] Charlson MEPP, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis* 1987;40:373–83.
- [13] Centraal bureau voor statistiek [1-1-2017]. Available from: <https://www.cbs.nl/>.
- [14] Perme MP, Stare J, Esteve J. On estimation in relative survival. *Biometrics* 2012;68(1):113–20.
- [15] Damhuis RA, Wereldsma JC, Wiggers T. The influence of age on resection rates and postoperative mortality in 6457 patients with colorectal cancer. *Int J Colorectal Dis* 1996;11(1):45–8.
- [16] Rutegard M, Haapamaki M, Matthiessen P, Rutegard J. Early postoperative mortality after surgery for rectal cancer in Sweden, 2000–2011. *Colorectal Dis* 2014;16(6):426–32.
- [17] Verweij NM, Schiphorst AH, Maas HA, Zimmerman DD, van den Bos F, Pronk A, et al. Colorectal cancer resections in the oldest old between 2011 and 2012 in The Netherlands. *Ann Surg Oncol* 2016;23(6):1875–82.
- [18] Breukink S, Pierie J, Wiggers T. Laparoscopic versus open total mesorectal excision for rectal cancer. *Cochrane Database Syst Rev* 2006;4:CD005200.
- [19] Ohtani H, Tamamori Y, Arimoto Y, Nishiguchi Y, Maeda K, Hirakawa K. A meta-analysis of the short- and long-term results of randomized controlled trials that compared laparoscopy-assisted and open colectomy for colon cancer. *J Cancer* 2012;3:49–57.
- [20] Gietelink L, Wouters MW, Bemelman WA, Dekker JW, Tollenaar RA, Tanis PJ, et al. Reduced 30-day mortality after laparoscopic colorectal cancer surgery: a population based study from the Dutch surgical colorectal audit (DSCA). *Ann Surg* 2016;264(1):135–40.
- [21] Bentrem DJ, Cohen ME, Hynes DM, Ko CY, Bilimoria KY. Identification of specific quality improvement opportunities for the elderly undergoing gastrointestinal surgery. *Arch Surg* 2009;144(11):1013–20.
- [22] Gooiker GA, Dekker JW, Bastiaannet E, van der Geest LG, Merkus JW, van de Velde CJ, et al. Risk factors for excess mortality in the first year after curative surgery for colorectal cancer. *Ann Surg Oncol* 2012;19(8):2428–34.
- [23] Ingraham AM, Cohen ME, Bilimoria KY, Feinglass JM, Richards KE, Hall BL, et al. Comparison of hospital performance in nonemergency versus emergency colorectal operations at 142 hospitals. *J Am Coll Surg* 2010;210(2):155–65.
- [24] Janssen-Heijnen ML, Maas HA, Houterman S, Lemmens VE, Rutten HJ, Coebergh JW. Comorbidity in older surgical cancer patients: influence on patient care and outcome. *Eur J Cancer* 2007;43(15):2179–93.
- [25] Read WL, Tierney RM, Page NC, Costas I, Govindan R, Spitznagel EL, et al. Differential prognostic impact of comorbidity. *J Clin Oncol* 2004;22(15):3099–103.
- [26] Robbins AS, Pavluck AL, Fedewa SA, Chen AY, Ward EM. Insurance status, comorbidity level, and survival among colorectal cancer patients age 18 to 64 years in the National Cancer Data Base from 2003 to 2005. *J Clin Oncol* 2009;27(22):3627–33.
- [27] Morris EJ, Sandin F, Lambert PC, Bray F, Klint A, Linklater K, et al. A population-based comparison of the survival of patients with colorectal cancer in England, Norway and Sweden between 1996 and 2004. *Gut* 2011;60(8):1087–93.

- [28] Dekker JW, Gooiker GA, Bastiaannet E, van den Broek CB, van der Geest LG, van de Velde CJ, et al. Cause of death the first year after curative colorectal cancer surgery; a prolonged impact of the surgery in elderly colorectal cancer patients. *Eur J Surg Oncol* 2014;40(11):1481–7.
- [29] Puig-La Calle Jr J, Quayle J, Thaler HT, Shi W, Paty PB, Quan SH, et al. Favorable short-term and long-term outcome after elective radical rectal cancer resection in patients 75 years of age or older. *Dis Colon Rectum* 2000;43(12):1704–9.
- [30] Violi V, Pietra N, Grattarola M, Sarli L, Choua O, Roncoroni L, et al. Curative surgery for colorectal cancer: long-term results and life expectancy in the elderly. *Dis Colon Rectum* 1998;41(3):291–8.
- [31] Maas HA, Lemmens VE, Nijhuis PH, de Hingh IH, Koning CC, Janssen-Heijnen ML. Benefits and drawbacks of short-course preoperative radiotherapy in rectal cancer patients aged 75 years and older. *Eur J Surg Oncol* 2013;39(10):1087–93.
- [32] Booth CM, Mackillop WJ. Translating new medical therapies into societal benefit: the role of population-based outcome studies. *J Am Med Assoc* 2008;300(18):2177–9.
- [33] Booth CM, Tannock IF. Evaluation of treatment benefit: randomized controlled trials and population-based observational research. *J Clin Oncol* 2013;31(26):3298–9.
- [34] D'Agostino Jr RB, D'Agostino Sr RB. Estimating treatment effects using observational data. *J Am Med Assoc* 2007;297(3):314–6.
- [35] Kristjansson SR, Nesbakken A, Jordhoy MS, Skovlund E, Audisio RA, Johannessen HO, et al. Comprehensive geriatric assessment can predict complications in elderly patients after elective surgery for colorectal cancer: a prospective observational cohort study. *Crit Rev Oncol Hematol* 2010;76(3):208–17.